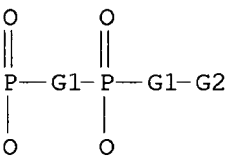
=> d que l1
L1 STR



G1 O,S,CH2,NH

G2 C,H,Ak,Cb

Structure attributes must be viewed using STN Express query preparation.

=> d his

(FILE 'HOME' ENTERED AT 19:37:54 ON 03 FEB 2003)

FILE 'REGISTRY' ENTERED AT 19:38:08 ON 03 FEB 2003
L1 STRUCTURE UPLOADED
L2 25326 L1 SSS FULL

FILE 'CAPLUS' ENTERED AT 19:38:37 ON 03 FEB 2003
L3 166197 L2
L4 95342 ANTICHOLINESTERASE OR ACETYLCHOLIN###### OR MUSCARIN? OR MACHR
L5 61 L4 (S) PYROPHOSPHAT?
L6 14 L5 AND L3
L7 0 L D6 TOTAL IBIB ABS HITSTR

=> d l6 total ibib abs hitstr

L6 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:816459 CAPLUS
DOCUMENT NUMBER: 135:339302
TITLE: Methods and compositions for enhancing cellular function through protection of tissue components
INVENTOR(S): Frey, William H., II; Fawcett, John Randall; Thorne, Robert Gary; Chen, Xueqing
PATENT ASSIGNEE(S): Healthpartners Research Foundation, USA
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 2001082932	A2	20011108	WO 2001-US13931	20010430	present application
WO 2001082932	A3	20020718			

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002028786	A1	20020307	US 2001-844450	20010427
EP 1278525	A2	20030129	EP 2001-930957	20010430

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.:

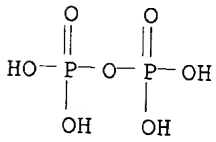
US 2000-200843P	P	20000501
US 2000-230263P	P	20000906
US 2000-233025P	P	20000915
US 2000-233263P	P	20000918
WO 2001-US13931	W	20010430

OTHER SOURCE(S): MARPAT 135:339302

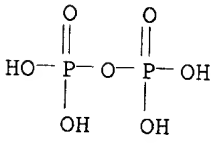
AB Methods and compns. for enhancing cellular function through protection of tissue components, such as receptors, proteins, lipids, nucleic acids, carbohydrates, hormones, vitamins, and cofactors, by administering pyrophosphate analogs or related compds. Preferably, the invention provides a method for protecting a muscarinic acetylcholine receptor (mAChR) an/or increasing the efficacy of and agent the directly or indirectly affects a mAChR in a subject in need thereof.

IT **2466-09-3**, Diphosphoric acid **2466-09-3D**, Diphosphoric acid, analogs **14127-68-5**, Tripolyphosphate **25612-73-1** **27590-04-1**, Imidodiphosphoric acid **34273-04-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for enhancing cellular function through protection of tissue components such as **muscarinic** receptors by administering **pyrophosphate** analogs and combination with other agents)

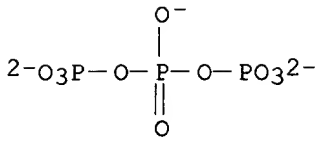
RN 2466-09-3 CAPLUS
CN Diphosphoric acid (9CI) (CA INDEX NAME)



RN 2466-09-3 CAPLUS
CN Diphosphoric acid (9CI) (CA INDEX NAME)

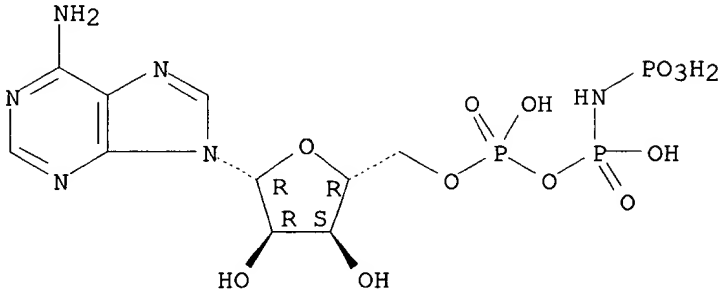


RN 14127-68-5 CAPLUS
CN Triphosphate (8CI, 9CI) (CA INDEX NAME)

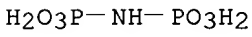


RN 25612-73-1 CAPLUS
CN 5'-Adenylic acid, monoanhydride with imidodiphosphoric acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

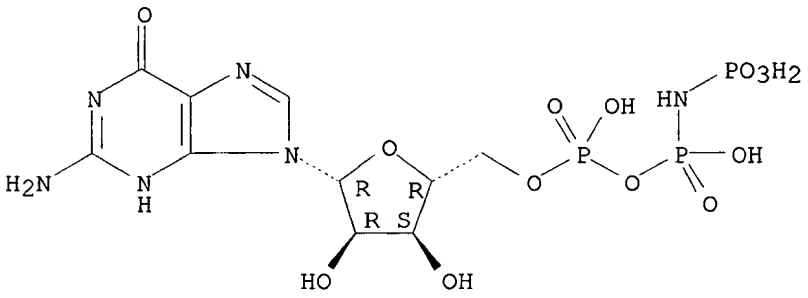


RN 27590-04-1 CAPLUS
CN Imidodiphosphoric acid (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 34273-04-6 CAPLUS
CN 5'-Guanylic acid, monoanhydride with imidodiphosphoric acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



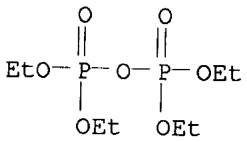
L6 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1973:119337 CAPLUS
DOCUMENT NUMBER: 78:119337
TITLE: Action of organophosphorus compounds on cell organelles. I. Effect of tetraethyldithiopyrophosphate on lysosomal hydrolases
AUTHOR(S): Barzu, Tereza; Cuparencu, Barbu; Hantz, Andrei
CORPORATE SOURCE: Dep. Pharmacol., Med. Pharm. Inst., Cluj, Rom.

SOURCE: Biochemical Pharmacology (1973), 22(2), 185-94
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Tetraethyl dithiopyrophosphate (TETPP) [3689-24-5], at doses which cause 50-80% acetylcholinesterase inhibition, increased the activity of rat brain acid phosphatase [9001-77-8] and liver acid phosphatase and β-glucuronidase [9001-45-0] both in vivo (3mg TETPP/kg, i.m.) and in vitro (10-6 to 10-3M TETPP). TETPP also caused labilization of the lysosomal membrane. In vitro studies with tetraethyl **pyrophosphate** [**107-49-3**], tetraethyl monothionopyrophosphate [645-78-3], and tetraethyl dithionopyrophosphate [3689-24-5] indicated little correlation between the **anticholinesterase** action of these compds. and the ability to activate lysosomal acid hydrolases, and the possibility of other mediating factors, especially the binding to organelle membranes, is discussed.

IT **107-49-3**
RL: BIOL (Biological study)
(acetylcholinesterase inhibition by, tetraethyl dithiopyrophosphate in relation to)

RN 107-49-3 CAPLUS
CN Diphosphoric acid, tetraethyl ester (9CI) (CA INDEX NAME)

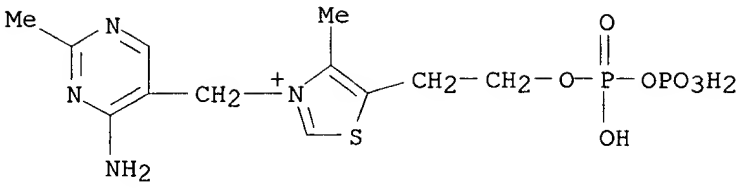


L6 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1972:429101 CAPLUS
DOCUMENT NUMBER: 77:29101
TITLE: Pharmacological actions of vitamin B1 and the related compounds
AUTHOR(S): Koda, Akihide; Nagai, Hiroichi; Watanabe, Shigekatsu
CORPORATE SOURCE: Gifu Pharm. Coll., Gifu, Japan
SOURCE: Gifu Yakka Daigaku Kiyo (1971), (20), 54-67
CODEN: GYDKA9; ISSN: 0434-0094
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

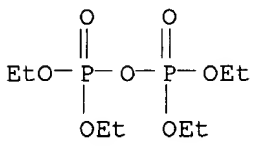
AB Thiamine propyl disulfide (I) [59-58-5] and thiamine **pyrophosphate** [**154-87-0**] potentiated **acetylcholine** [51-84-3]-induced spasm of the isolated guinea pig ileum at 0.1-1μM, increased the formation of both free and total **acetylcholine** in minced frog brain at 0.1-50μM, and inhibited cholinesterase [9001-08-5] of horse serum at >0.1mM. The potentiating effect of these compds. may be due to their enhancement of acetylcholine synthesis rather than their inhibiting action on cholinesterase.

IT **154-87-0**
RL: BIOL (Biological study)
(acetylcholine formation and pharmacol. response to)

RN 154-87-0 CAPLUS
CN Thiazolium, 3-[(4-amino-2-methyl-5-pyrimidinyl)methyl]-4-methyl-5-(4,6,6-trihydroxy-4,6-dioxido-3,5-dioxa-4,6-diphosphahex-1-yl)-, chloride (9CI) (CA INDEX NAME)



L6 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1972:95448 CAPLUS
DOCUMENT NUMBER: 76:95448
TITLE: Influence of an oxime on the release of acetylcholine into perfused cerebral ventricles
AUTHOR(S): Edery, H.
CORPORATE SOURCE: Israel Inst. Biol. Res., Ness-Ziona, Israel
SOURCE: Drugs Cholinergic Mech. CNS (Cent. Nerv. Syst.), Proc. Conf. (1970), 411-18. Editor(s): Heilbronn, Edith. Foersvarets Forskningsanst.: Stockholm, Swed.
CODEN: 24HKAN
DOCUMENT TYPE: Conference
LANGUAGE: English
AB 4-Hydroxyiminomethyl-1-[3-(N,N-dimethylamino)propyl]pyridinium chloride hydrochloride (I) [15682-12-9] is an antidote for organophosphate poisoning. In cats, i.v. or intraventricular I greatly reduced the **acetylcholine** [51-84-3] content of the perfusate during ventriculocisternal perfusion with a fluid containing tetraethyl **pyrophosphate** (TEPP) [**107-49-3**]. Plasma cholinesterase [9001-08-5] decreased gradually, and was subsequently reactivated after i.v., but not intraventricular, administration of I.
IT **107-49-3**
RL: BIOL (Biological study)
(hydroxyiminomethyl[(dimethylamino)propyl]pyridinium chloride hydrochloride effect on acetylcholine of brain in relation to)
RN 107-49-3 CAPLUS
CN Diphosphoric acid, tetraethyl ester (9CI) (CA INDEX NAME)



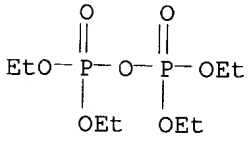
L6 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1968:494754 CAPLUS
DOCUMENT NUMBER: 69:94754
TITLE: Effects of physostigmine on the after-discharge and slow postsynaptic potentials of bullfrog sympathetic ganglia
AUTHOR(S): Koketsu, K.; Nishi, S.; Noda, Y.

CORPORATE SOURCE: Stritch Sch. of Med., Loyola Univ., Hines, IL, USA
SOURCE: British Journal of Pharmacology (1968), 34(1), 177-88
CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of **anticholinesterases** (I) (physostigmine, prostigmine, and tetraethyl **pyrophosphate**) on the afterdischarges and the extracellular and intracellular slow potentials of bullfrog sympathetic ganglia were studied. The I augmented the early afterdischarge, the late neg. potential, and the slow excitatory postsynaptic potential. This indicated that the nature of the early afterdischarge was cholinergic (muscarinic) and that the late neg. potential or the slow excitatory postsynaptic potential generated the early afterdischarge. Since the I increased the pos. potential, the depression of the early afterdischarge observed in the presence of a I was explained to be caused by the increased inhibitory effect of the enhanced pos. potential. Prostigmine and tetraethyl pyrophosphate did not show any appreciable effects on the late afterdischarge, the late late neg. potential, or the late slow excitatory postsynaptic potential. This indicated that the nature of the late afterdischarge was noncholinergic and that the late late neg. potential or the late slow excitatory postsynaptic potential generated the late afterdischarge. Physostigmine reversibly depressed the late afterdischarge, the late late neg. potential, and the late slow excitatory postsynaptic potential. The depressant action of physostigmine was not due to its I action.

IT **107-49-3**
RL: BIOL (Biological study)
(nerve center potential response to)

RN 107-49-3 CAPLUS
CN Diphosphoric acid, tetraethyl ester (9CI) (CA INDEX NAME)



L6 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1968:417982 CAPLUS
DOCUMENT NUMBER: 69:17982
TITLE: Central nervous system depressant modifiers
INVENTOR(S): Proctor, Charles D.
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3382147	A	19680507	US 1962-179157	19620312

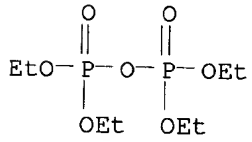
PRIORITY APPLN. INFO.: US 1962-179157 19620312

AB Tranquilizers, barbiturate hypnotics, and other central nervous system depressants are potentiated in their activity by **anticholinesterases** such as tetraethyl **pyrophosphate**

(I), O,O-diethyl O-(p-nitrophenyl)thiophosphate, or diisopropyl fluorophosphate. I may be injected in aqueous solution, in poly(ethylene glycol), or propylene glycol and enhances and prolongs the activity of these drugs.

IT **107-49-3**
RL: BIOL (Biological study)
(nervous system depressants, potentiation by)

RN 107-49-3 CAPLUS
CN Diphosphoric acid, tetraethyl ester (9CI) (CA INDEX NAME)



L6 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2003 ACS

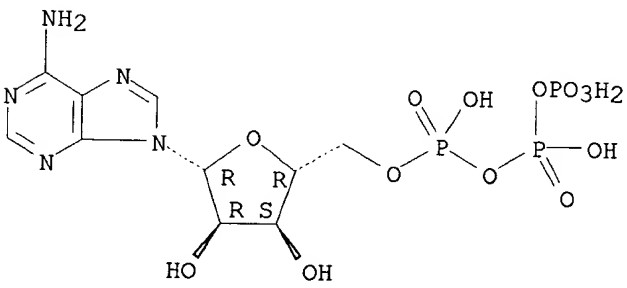
ACCESSION NUMBER:	1965:39383 CAPLUS
DOCUMENT NUMBER:	62:39383
ORIGINAL REFERENCE NO.:	62:6973b-d
TITLE:	The mechanism whereby certain nucleotides produce contractions of smooth muscle
AUTHOR(S):	Daniel, E. E.; Irwin, John
CORPORATE SOURCE:	Univ. Alberta, Edmonton
SOURCE:	Can. J. Physiol. Pharmacol. (1965), 43(1), 89-109
DOCUMENT TYPE:	Journal
LANGUAGE:	Unavailable

AB ATP and ADP were about equally effective in causing contraction of rat uterine muscle, and were much more effective than AMP and adenosine. Orthophosphate and pyrophosphate were less effective. None of the nucleotides caused inhibition of contraction to other drugs such as acetylcholine. Neither selective inhibition of known receptors nor depolarization by K2SO4 prevented these contractions, but Ca depletion sufficient to prevent acetylcholine contractions prevented ATP and ADP contractions. Exptl. results indicated that the nucleotides might have acted by virtue of their ability to complex Mg present in the cell membrane, thereby favoring Ca entry and contraction. Substitution of Sr for Ca enhanced the effectiveness of ATP in evoking contractions.

IT **56-65-5**, Adenosine, triphosphate **58-64-0**, Adenosine pyrophosphate
(uterus contractile response to)

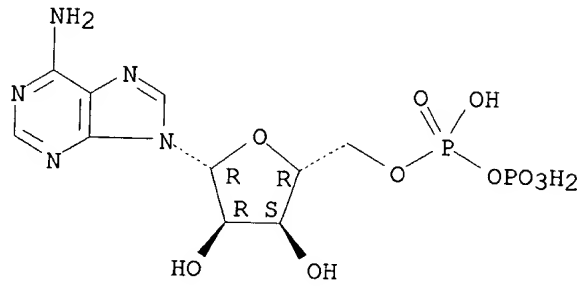
RN 56-65-5 CAPLUS
CN Adenosine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



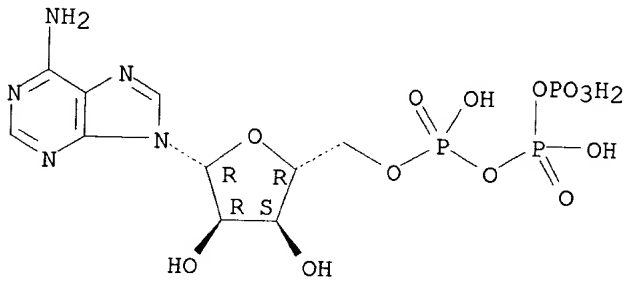
RN 58-64-0 CAPLUS
CN Adenosine 5'-(trihydrogen diphosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **56-65-5**, Adenosine triphosphate
(uterus response to)
RN 56-65-5 CAPLUS
CN Adenosine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



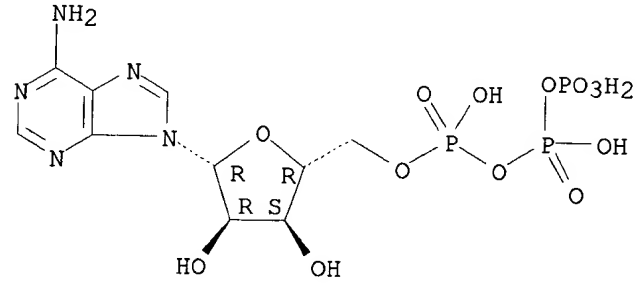
L6 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1964:407045 CAPLUS
DOCUMENT NUMBER: 61:7045
ORIGINAL REFERENCE NO.: 61:1142h
TITLE: Effect of purines on the acetylcholine content of rat brain
AUTHOR(S): Bose, B. C.; Saifi, A. Q.; Ray, N. M.
CORPORATE SOURCE: M.G.M. Med. Coll., Indore
SOURCE: Current Sci. (India) (1964), 33(7), 212
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB The average acetylcholine (I) content in brain tissue of control rats was 2.46 γ/g. The I content of the brain after acute administration of the following purine derivs. was: theophylline, 4.12 ± 0.12; theobromine, 2.48 ± 0.43; adenosine diphosphate, 2.06 ± 0.18; adenosine triphosphate, 1.83 ± 0.29; and caffeine, 1.60 ± 0.20 γ/g. On chronic administration, none of the above drugs influence the I level of brain tissue.

IT **56-65-5**, Adenosine triphosphate **58-64-0**, Adenosine **pyrophosphate**
(**acetylcholine** in brain after administration of)
RN 56-65-5 CAPLUS

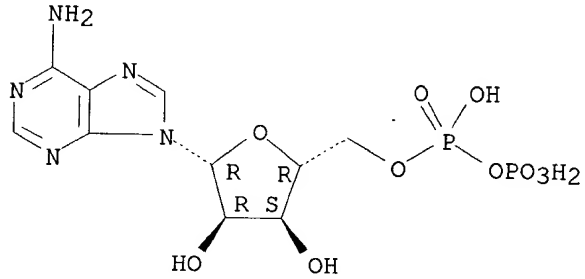
CN Adenosine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 58-64-0 CAPLUS
CN Adenosine 5'-(trihydrogen diphosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:	1961:3812 CAPLUS
DOCUMENT NUMBER:	55:3812
ORIGINAL REFERENCE NO.:	55:780i,781a-c
TITLE:	Cholinesterase inhibition and spontaneous activity of the frog rectus abdominis muscle
AUTHOR(S):	Kraatz, C. P.
CORPORATE SOURCE:	Jefferson Med. Coll., Philadelphia, PA
SOURCE:	J. Pharmacol. Exptl. Therap. (1960), 130, 194-203
DOCUMENT TYPE:	Journal
LANGUAGE:	Unavailable

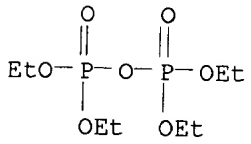
AB Inhibition of the cholinesterase of the isolated frog rectus abdominis muscle leads to spontaneous shortening. The effectiveness of various inhibitors in evoking such activity generally parallels their ability to sensitize the muscle to **acetylcholine**, with tetraethyl **pyrophosphate** (TEPP) most consistently active and neostigmine somewhat inferior. The property is manifested in varying degrees by unsym. diethyl bis(dimethylamido)pyrophosphate (B-6515), pyridostigmine, and edrophonium, while octamethyl pyrophosphoroamide and physostigmine are ineffective. Spontaneous contractions in 10-6 dilution TEPP or 10-5 B-6515 occur only after approx. 90% of the cholinesterase of the muscle has been inactivated. Localization expts. and inhibition by curare and other drugs that depress the responses to acetylcholine indicate that a fully sensitive neuromuscular junction is essential for development of the activity. The twitch and tonus components are both brought into activity

by minimal concns. of TEPP, while the other inhibitors at comparable levels activate principally twitch fibers.

IT **107-49-3**, Ethyl pyrophosphate, Et4P2O7
(cholinesterase inhibition by, muscle spontaneous activity and)

RN 107-49-3 CAPLUS

CN Diphosphoric acid, tetraethyl ester (9CI) (CA INDEX NAME)



L6 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1959:57851 CAPLUS

DOCUMENT NUMBER: 53:57851

ORIGINAL REFERENCE NO.: 53:10508h-i

TITLE: Action of anticholinesterases on the bronchial muscle of the guinea pig: sensitization to acetylcholine and histamine

AUTHOR(S): Chary, R.; Bocquet, P.; Jayot, R.

CORPORATE SOURCE: Centre etudes Bouchet, Paris

SOURCE: J. physiol. (Paris) (1958), 50, 215-19

DOCUMENT TYPE: Journal

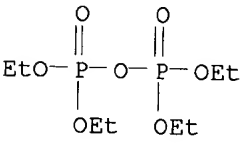
LANGUAGE: Unavailable

AB cf. C.A. 52, 18853g. In mg./kg. body weight concns. isopropyl phosphorofluoridate (0.010), eserine salicylate (0.025), ethyl phosphoramidocyanidate, and tetraethyl **pyrophosphate** (I) (0.025) augmented the bronchoconstrictor effect of **acetylcholine**. All except I sensitized the similar effect of histamine.

IT **107-49-3**, Ethyl **pyrophosphate**, Et4P2O7
(effect on bronchial constrictor effect of **acetylcholine** and histamine)

RN 107-49-3 CAPLUS

CN Diphosphoric acid, tetraethyl ester (9CI) (CA INDEX NAME)



L6 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1959:41670 CAPLUS

DOCUMENT NUMBER: 53:41670

ORIGINAL REFERENCE NO.: 53:7496f-h

TITLE: **Acetylcholine** in Periplaneta americana. III. **Acetylcholine** in roaches treated with tetraethyl **pyrophosphate** and 2,2-bis(p-chlorophenyl)-1,1,1-trichloroethane

AUTHOR(S): Colhoun, E. H.

CORPORATE SOURCE: Sci. Serv. Lab., London

SOURCE: Can. J. Biochem. and Physiol. (1959), 37, 259-72

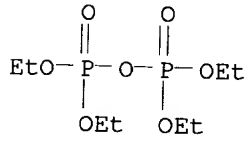
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB cf. C.A. 52, 17539e. The levels of **acetylcholine** (ACh) in the thoracic nerve cords of cockroaches were increased by the topical application of DDT and of tetraethyl **pyrophosphate** (TEPP), but only TEPP inhibited cholinesterase (ChE). Improvements in the correlation of symptoms, nervous activity, and ACh levels with ChE were obtained when nerve cords were homogenized in saline containing ACh, which prevented further inhibition of ChE by TEPP found to be present in blood and nervous tissue. There was a similarity in the distribution of ACh in thoracic nerve cords of roaches after topical treatment with TEPP and DDT, but the physiol. properties of the blood revealed differences in the mode of action of the 2 insecticides.

IT **107-49-3**, Ethyl **pyrophosphate**, Et4P2O7
(**acetylcholine** in cockroach after treatment with)

RN 107-49-3 CAPLUS

CN Diphosphoric acid, tetraethyl ester (9CI) (CA INDEX NAME)



L6 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1958:105768 CAPLUS

DOCUMENT NUMBER: 52:105768

ORIGINAL REFERENCE NO.: 52:18749a-c

TITLE: Relaxing action of sodium phosphate, **pyrophosphate**, urea, or ethylenediaminetetraacetate upon **acetylcholine** -contracture of living skeletal muscle. I. Relaxative effect of sodium phosphate on **acetylcholine** -contracture of living skeletal muscle

AUTHOR(S): Urata, Tatsuo

CORPORATE SOURCE: Univ. Kumamoto

SOURCE: Kumamoto Med. J. (1957), 10, 60-5

DOCUMENT TYPE: Journal

LANGUAGE: English

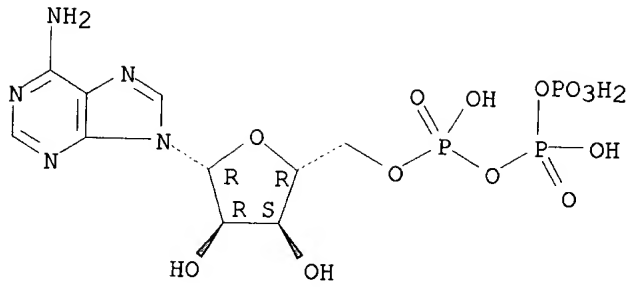
AB Na2HPO4 (I) relaxes muscle contracted by acetylcholine, as does adenosine triphosphate (ATP). The relaxing action of I is synergistic with that of ATP.

IT **56-65-5**, Adenosine triphosphate
(in muscle relaxation)

RN 56-65-5 CAPLUS

CN Adenosine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



(synergism with Na2HPO4 on acetylcholine-contracted muscle

L6 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1958:57677 CAPLUS
DOCUMENT NUMBER: 52:57677
ORIGINAL REFERENCE NO.: 52:10417e-i,10418a
TITLE: Effects in man of the anticholinesterase compound, sarin
AUTHOR(S): Grob, David; Harvey, John C.
CORPORATE SOURCE: Johns Hopkins Univ., Baltimore, MD
SOURCE: J. Clin. Invest. (1958), 37, 350-68
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

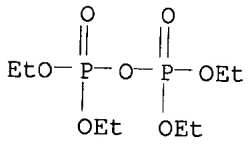
AB The administration of sarin to normal subjects resulted in muscarine-like, nicotine-like, and central nervous system signs and symptoms attributable to the inhibition of cholinesterase enzymes in the effector tissues, and resembling those produced by other organic phosphate anticholinesterase compds. Of the compds. studied, sarin had the greatest anticholinesterase activity in vitro. It is the most toxic to animals. Very small doses produced pharmacologic effects in man. Tetraethylpyrophosphate (TPP), and diisopropylfluorophosphate (DFP), and parathion are less potent in this order. Sarin resembled DFP and parathion in being more soluble in lipoid than in aqueous medium, and in producing marked central neural effects. It resembles DFP in producing irreversible inhibition of cholinesterase enzymes in vitro, and probably of plasma and red cell cholinesterase activity in vivo. The relation between the dose of sarin and the degree of depression of cholinesterase activity was the same in vitro as it was for plasma and red cell cholinesterase activity in vivo. The amount of enzyme inhibited by a given dose was proportional to the level of enzyme activity; each increment in dose inhibited the same fraction of enzyme; and the log of the fraction that remained active decreased linearly with increasing dose. When sarin was administered in repeated doses at intervals of several hrs. to 1 day, the effect on cholinesterase activity and on symptoms was cumulative. Oral administration of sarin resulted in systemic effects, and perhaps local gastrointestinal actions. Intraarterial injections produced local and systemic effects. Conjunctival instillation resulted in local ocular changes. The effects of sarin were very prolonged, lasting from several hrs. after the smallest effective doses to several days after doses which produced moderate symptoms. The administration of atropine ameriolated the muscarin-like effects of sarin, the central neural effects, but had no influence on muscular weakness. There was reduced susceptibility to the action of atropine in the presence of symptoms due to sarin. Following depression by sarin, the cholesterolase activity of the plasma was restored over a period of 40 days, at a rate comparable to a regeneration of the enzyme by the liver, while that of the red blood cells was restored at the rate of 1% per day, suggestive of regeneration of enzyme in newly formed red blood

cells. 32 references.

IT **107-49-3**, Ethyl **pyrophosphate**, Et4P2O7
(toxicity of, compared with sarin and other **anticholinesterase** compds.)

RN 107-49-3 CAPLUS

CN Diphosphoric acid, tetraethyl ester (9CI) (CA INDEX NAME)



L6 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1958:36919 CAPLUS

DOCUMENT NUMBER: 52:36919

ORIGINAL REFERENCE NO.: 52:6653a-c

TITLE: Tetraethyl **pyrophosphate** and **acetylcholine** in Periplaneta americana

AUTHOR(S): Colhoun, E. H.

CORPORATE SOURCE: Sci. Serv. Lab., London, Can.

SOURCE: Science (1958), 127, 25

DOCUMENT TYPE: Journal

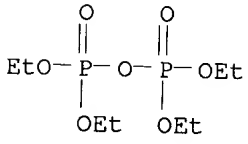
LANGUAGE: Unavailable

AB Male roaches were treated topically with lethal doses (5 γ per roach) of tetraethyl pyrophosphate (I). The acetylcholine (II) content of thoracic cords was determined, and electrophysiol. observations were made on the gross nerve activity of the ventral cord. Two peaks of content of II were found. The 1st, at 1/2 hr. and 20% above the normal of 79 γ/g., coincided with a period of intense nervous activity. The 2nd, 120% above normal, occurred at 24 hrs. From then on, the roaches showed signs of necrosis, and at 48 hrs., the content of II had fallen to 0. Blood of normal roaches had no II, but blood of roaches treated with I contained II. DDT-treated roaches had no II in the blood and only normal amts. of II in the thoracic cords. There is a specific difference in the mode of action of these 2 insecticides.

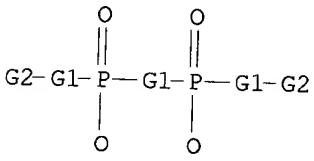
IT **107-49-3**, Ethyl **pyrophosphate**, Et4P2O7
(**acetylcholine** in cockroach after treatment with)

RN 107-49-3 CAPLUS

CN Diphosphoric acid, tetraethyl ester (9CI) (CA INDEX NAME)



=> d que l1
L1 STR



G1 O,S,CH2,NH

G2 C,H,Ak,Cb

Structure attributes must be viewed using STN Express query preparation.

=> d his

(FILE 'HOME' ENTERED AT 18:50:56 ON 03 FEB 2003)

FILE 'REGISTRY' ENTERED AT 18:51:09 ON 03 FEB 2003
L1 STRUCTURE UPLOADED
L2 25326 L1 SSS FULL

FILE 'CAPLUS' ENTERED AT 18:51:38 ON 03 FEB 2003
L3 166197 L2
L4 165908 MUSCARIN? OR ACETYLCHOLIN? OR CHOLIN? OR NEUROTROPH? OR NEURITO
L5 4339 L3 AND L4
L6 0 L4 (S) PHYRPHOSPHAT?
L7 307 L4 (S) PYROPHOSPHAT?
L8 102 L7 AND L3
L9 100 L8 NOT PY>=2000
L10 100 DUP REM L9 (0 DUPLICATES REMOVED)
L11 107071 MUSCARIN? OR ACETYLCHOLIN? OR NEUROTROPH? OR NEURITOGEN?
L12 97 L11 (S) PYROPHOSPHAT?
L13 20 L12 AND L3
L14 19 L13 NOT PY>=2000
L15 19 FOCUS L14 1-

=> d l15 total ibib abs hitstr

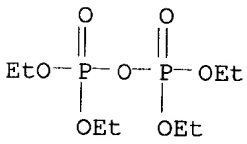
L15 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1959:41670 CAPLUS
DOCUMENT NUMBER: 53:41670
ORIGINAL REFERENCE NO.: 53:7496f-h
TITLE: **Acetylcholine** in Periplaneta americana. III. **Acetylcholine** in roaches treated with tetraethyl **pyrophosphate** and 2,2-bis(p-chlorophenyl)-1,1,1-trichloroethane
AUTHOR(S): Colhoun, E. H.
CORPORATE SOURCE: Sci. Serv. Lab., London
SOURCE: Can. J. Biochem. and Physiol. (1959), 37, 259-72
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C.A. 52, 17539e. The levels of **acetylcholine** (ACh) in the thoracic nerve cords of cockroaches were increased by the topical application of DDT and of tetraethyl **pyrophosphate** (TEPP), but only TEPP inhibited cholinesterase (ChE). Improvements in the correlation of symptoms, nervous activity, and ACh levels with ChE were obtained when

nerve cords were homogenized in saline containing ACh, which prevented further inhibition of ChE by TEPP found to be present in blood and nervous tissue. There was a similarity in the distribution of ACh in thoracic nerve cords of roaches after topical treatment with TEPP and DDT, but the physiol. properties of the blood revealed differences in the mode of action of the 2 insecticides.

IT **107-49-3**, Ethyl **pyrophosphate**, Et4P2O7
(**acetylcholine** in cockroach after treatment with)

RN 107-49-3 CAPLUS

CN Diphosphoric acid, tetraethyl ester (9CI) (CA INDEX NAME)



L15 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1958:36919 CAPLUS

DOCUMENT NUMBER: 52:36919

ORIGINAL REFERENCE NO.: 52:6653a-c

TITLE: Tetraethyl **pyrophosphate** and **acetylcholine** in Periplaneta americana

AUTHOR(S): Colhoun, E. H.

CORPORATE SOURCE: Sci. Serv. Lab., London, Can.

SOURCE: Science (1958), 127, 25

DOCUMENT TYPE: Journal

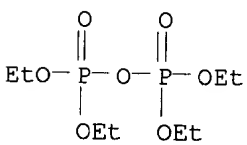
LANGUAGE: Unavailable

AB Male roaches were treated topically with lethal doses (5 γ per roach) of tetraethyl pyrophosphate (I). The acetylcholine (II) content of thoracic cords was determined, and electrophysiol. observations were made on the gross nerve activity of the ventral cord. Two peaks of content of II were found. The 1st, at 1/2 hr. and 20% above the normal of 79 γ/g., coincided with a period of intense nervous activity. The 2nd, 120% above normal, occurred at 24 hrs. From then on, the roaches showed signs of necrosis, and at 48 hrs., the content of II had fallen to 0. Blood of normal roaches had no II, but blood of roaches treated with I contained II. DDT-treated roaches had no II in the blood and only normal amts. of II in the thoracic cords. There is a specific difference in the mode of action of these 2 insecticides.

IT **107-49-3**, Ethyl **pyrophosphate**, Et4P2O7
(**acetylcholine** in cockroach after treatment with)

RN 107-49-3 CAPLUS

CN Diphosphoric acid, tetraethyl ester (9CI) (CA INDEX NAME)



L15 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2003 ACS

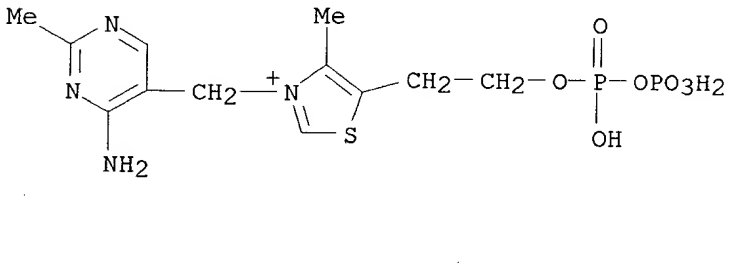
ACCESSION NUMBER: 1972:429101 CAPLUS

DOCUMENT NUMBER: 77:29101
TITLE: Pharmacological actions of vitamin B1 and the related compounds
AUTHOR(S): Koda, Akihide; Nagai, Hiroichi; Watanabe, Shigekatsu
CORPORATE SOURCE: Gifu Pharm. Coll., Gifu, Japan
SOURCE: Gifu Yakka Daigaku Kiyo (1971), (20), 54-67
CODEN: GYDKA9; ISSN: 0434-0094
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB Thiamine propyl disulfide (I) [59-58-5] and thiamine **pyrophosphate** [**154-87-0**] potentiated **acetylcholine** [51-84-3]-induced spasm of the isolated guinea pig ileum at 0.1-1μM, increased the formation of both free and total **acetylcholine** in minced frog brain at 0.1-50μM, and inhibited cholinesterase [9001-08-5] of horse serum at >0.1mM. The potentiating effect of these compds. may be due to their enhancement of acetylcholine synthesis rather than their inhibiting action on cholinesterase.

IT **154-87-0**
RL: BIOL (Biological study)
(acetylcholine formation and pharmacol. response to)

RN 154-87-0 CAPLUS
CN Thiazolium, 3-[(4-amino-2-methyl-5-pyrimidinyl)methyl]-4-methyl-5-(4,6,6-trihydroxy-4,6-dioxido-3,5-dioxa-4,6-diphosphahex-1-yl)-, chloride (9CI) (CA INDEX NAME)



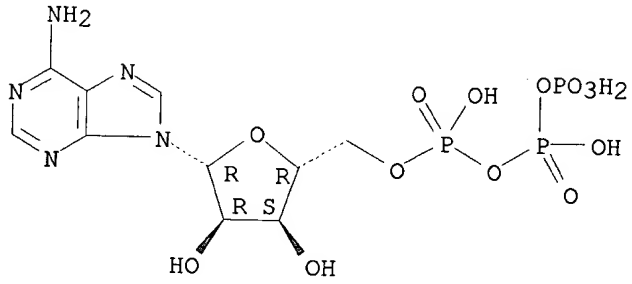
L15 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1958:105768 CAPLUS
DOCUMENT NUMBER: 52:105768
ORIGINAL REFERENCE NO.: 52:18749a-c
TITLE: Relaxing action of sodium phosphate, **pyrophosphate**, urea, or ethylenediaminetetraacetate upon **acetylcholine** -contracture of living skeletal muscle. I. Relaxative effect of sodium phosphate on **acetylcholine** -contracture of living skeletal muscle
AUTHOR(S): Urata, Tatsuo
CORPORATE SOURCE: Univ. Kumamoto
SOURCE: Kumamoto Med. J. (1957), 10, 60-5
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Na2HPO4 (I) relaxes muscle contracted by acetylcholine, as does adenosine triphosphate (ATP). The relaxing action of I is synergistic with that of ATP.

IT **56-65-5**, Adenosine triphosphate

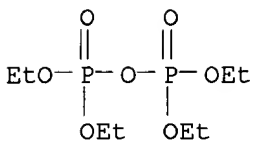
(in muscle relaxation)
RN 56-65-5 CAPLUS
CN Adenosine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



(synergism with Na2HPO4 on acetylcholine-contracted muscle

L15 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1971:474420 CAPLUS
DOCUMENT NUMBER: 75:74420
TITLE: Species differences in the rates of reaction of diaphragm particulate **acetylcholinesterases** with tetraethyl **pyrophosphate** and pralidoxime
AUTHOR(S): Berry, W. K.
CORPORATE SOURCE: Chem. Def. Establ., Porton Down/Wilts., UK
SOURCE: Biochemical Pharmacology (1971), 20(6), 1333-4
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB In rats and guinea pigs, a major factor in the species different TEPP (tetraethyl **pyrophosphate**) (I) protection of diaphragm particulate **acetylcholinesterases** from Soman (1,2,2-trimethylpropyl methylphosphonofluoridate) was the speed of the inhibition and reactivation processes; inhibition by I was slower in guinea pig prepns. than in those from the rat. The reactivation of the acetylcholinesterases by P2S (2-hydroxyiminomethyl-N-methylpyridinium methanesulfonate) lagged behind the clearance of Soman from the guinea pig diaphragm, while it was ineffective in the rat because the rapid reactivation occurred while there was still enough free Soman present to reinhibit the reactivated fraction of enzyme. Similarly rapid reactivation by TMB-4 (1,3-di(4-hydroxyiminomethylpyridinium)propane dihalide) may explain its therapeutic ineffectiveness in the guinea pig when used in this manner.
IT **107-49-3**
RL: BIOL (Biological study)
(acetylcholinesterase reaction with, species differences in)
RN 107-49-3 CAPLUS
CN Diphosphoric acid, tetraethyl ester (9CI) (CA INDEX NAME)

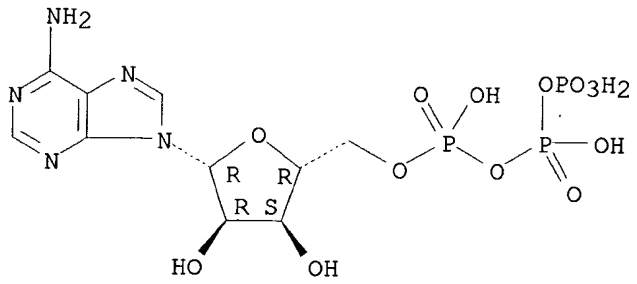


L15 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1973:542779 CAPLUS
DOCUMENT NUMBER: 79:142779
TITLE: Oxime analogs of physostigmine
AUTHOR(S): Wells, J. N.; Davisson, J. N.; Campbell, W. R.; Sangiah, S.; Yim, G. K. W.
CORPORATE SOURCE: Dep. Med. Chem., Purdue Univ., Lafayette, IN, USA
SOURCE: Journal of Medicinal Chemistry (1973), 16(6), 700-3
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The oxime analog of physostigmine, 5-acetyl-1,3a, 8-trimethyl-2,3,3a,8a-tetrahydropyrrolo[2,3-b]indole oxime (I) [41934-76-3] (200 mg/kg i.p.), did not protect mice from the lethal effects of tetraethyl **pyrophosphate** [**107-49-3**], an **acetylcholinesterase** inhibitor. I and 5-acetyl-3-(2-dimethylaminoethyl)-1,3-dimethylindoline oxime (II) [41934-77-4] produced little and no reactivation in vitro, resp., of bovine erythrocyte acetylcholinesterase [9000-81-1] poisoned with paraoxon. To synthesize I, 1,3-dimethyloxindole [24438-17-3] was 5-acetylated, reacted with 1,2-dibromoethane [106-93-4] in NaOEt-EtOH to form 5-acetyl-3-(2-bromoethyl)-1,3-dimethyloxindole [41934-79-6], converted to the ethylene ketal, then to the 3-(2-methylaminoethyl) derivative, cyclized with LiAlH4, hydrolyzed, and reacted with NH2OH to give I. Similar results were obtained with the hydroxy analogs 5-(1-hydroxyethyl)-1,3a,8-trimethyl-2,3,3a,8a-tetrahydropyrrolo[2,3-b]indole [41934-80-9] and 5-(1-hydroxyethyl)-3-(2-dimethylaminoethyl)-1,3-dimethylindoline [41934-81-0].

L15 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1965:39383 CAPLUS
DOCUMENT NUMBER: 62:39383
ORIGINAL REFERENCE NO.: 62:6973b-d
TITLE: The mechanism whereby certain nucleotides produce contractions of smooth muscle
AUTHOR(S): Daniel, E. E.; Irwin, John
CORPORATE SOURCE: Univ. Alberta, Edmonton
SOURCE: Can. J. Physiol. Pharmacol. (1965), 43(1), 89-109
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB ATP and ADP were about equally effective in causing contraction of rat uterine muscle, and were much more effective than AMP and adenosine. Orthophosphate and pyrophosphate were less effective. None of the nucleotides caused inhibition of contraction to other drugs such as acetylcholine. Neither selective inhibition of known receptors nor depolarization by K2SO4 prevented these contractions, but Ca depletion sufficient to prevent acetylcholine contractions prevented ATP and ADP contractions. Exptl. results indicated that the nucleotides might have acted by virtue of their ability to complex Mg present in the cell membrane, thereby favoring Ca entry and contraction. Substitution of Sr for Ca enhanced the effectiveness of ATP in evoking contractions.

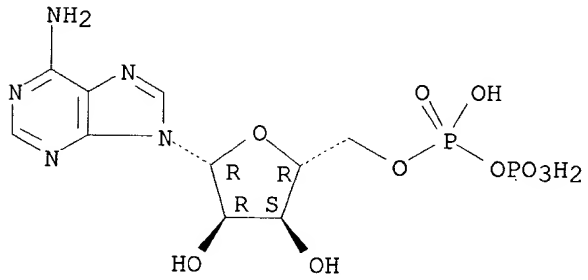
IT **56-65-5**, Adenosine, triphosphate **58-64-0**, Adenosine pyrophosphate
(uterus contractile response to)
RN 56-65-5 CAPLUS
CN Adenosine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



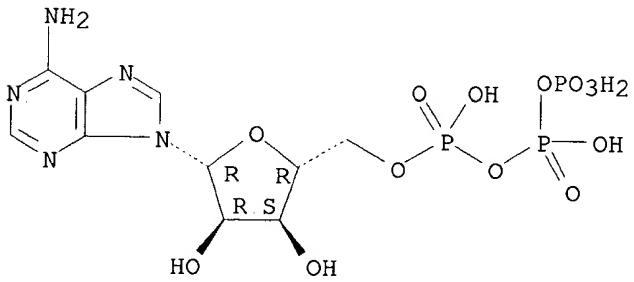
RN 58-64-0 CAPLUS
CN Adenosine 5'-(trihydrogen diphosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **56-65-5**, Adenosine triphosphate
(uterus response to)
RN 56-65-5 CAPLUS
CN Adenosine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L15 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1958:41789 CAPLUS

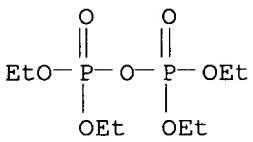
DOCUMENT NUMBER: 52:41789
ORIGINAL REFERENCE NO.: 52:7531f-h
TITLE: Designing of a new drug with antidotal properties against the nerve-gas sarin (isopropyl methylphosphonofluoridate)
AUTHOR(S): Wilson, Irwin B.
CORPORATE SOURCE: Columbia Univ.
SOURCE: Biochim. et Biophys. Acta (1958), 27, 196-9
DOCUMENT TYPE: Journal
LANGUAGE: English

AB cf. C.A. 51, 16945d. 2-Pyridinealdoxime dodecyl iodide (I) was prepared expecting that it would be much more lipide-soluble than the methiodide (II) and would, therefore, penetrate tissues, in vivo, which were not permeable to II; if such were the case I might augment the antidotal properties of II in those instances of alkylphosphate intoxication in which the significant area of penetration of the poison did not lie entirely within the sphere of penetration of II. II was readily soluble in H2O and very poorly soluble in CHCl3, and I showed the reverse. I was about 1/3 as active as II as an in vitro reactivator of tetraethyl **pyrophosphate** -inhibited **acetylcholinesterase**, compared at a concentration of 5 + 10-6M. I considerably extended the antidotal properties of II plus atropine when administered to white mice poisoned with sarin.

IT **107-49-3**, Ethyl **pyrophosphate**, Et4P2O7
(**acetylcholinesterase** inhibition by, reactivation by 2-pyridinealdoxime dodecyl iodide)

RN 107-49-3 CAPLUS

CN Diphosphoric acid, tetraethyl ester (9CI) (CA INDEX NAME)



L15 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1972:95448 CAPLUS
DOCUMENT NUMBER: 76:95448
TITLE: Influence of an oxime on the release of acetylcholine into perfused cerebral ventricles
AUTHOR(S): Edery, H.
CORPORATE SOURCE: Israel Inst. Biol. Res., Ness-Ziona, Israel
SOURCE: Drugs Cholinergic Mech. CNS (Cent. Nerv. Syst.), Proc. Conf. (1970), 411-18. Editor(s): Heilbronn, Edith. Foersvarets Forskningsanst.: Stockholm, Swed. CODEN: 24HKAN
DOCUMENT TYPE: Conference
LANGUAGE: English

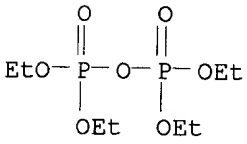
AB 4-Hydroxyiminomethyl-1-[3-(N,N-dimethylamino)propyl]pyridinium chloride hydrochloride (I) [15682-12-9] is an antidote for organophosphate poisoning. In cats, i.v. or intraventricular I greatly reduced the **acetylcholine** [51-84-3] content of the perfusate during ventriculocisternal perfusion with a fluid containing tetraethyl **pyrophosphate** (TEPP) [**107-49-3**]. Plasma cholinesterase [9001-08-5] decreased gradually, and was subsequently reactivated after i.v., but not intraventricular, administration of I.

IT **107-49-3**

RL: BIOL (Biological study)
(hydroxyiminomethyl[(dimethylamino)propyl]pyridinium chloride hydrochloride effect on acetylcholine of brain in relation to)

RN 107-49-3 CAPLUS

CN Diphosphoric acid, tetraethyl ester (9CI) (CA INDEX NAME)



L15 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1987:437049 CAPLUS

DOCUMENT NUMBER: 107:37049

TITLE: Effect of thiamin and its derivatives on the acetylcholinesterase activity in the brain and blood of albino mice

AUTHOR(S): Petrov, S. A.; Rozanov, A. Ya.; Tishchenko, D. V.

CORPORATE SOURCE: I. I. Mechnikov Univ., Odessa, USSR

SOURCE: Ukrainskii Biokhimicheskii Zhurnal (1978-1999) (1987), 59(3), 76-9
CODEN: UBZHD4; ISSN: 0201-8470

DOCUMENT TYPE: Journal

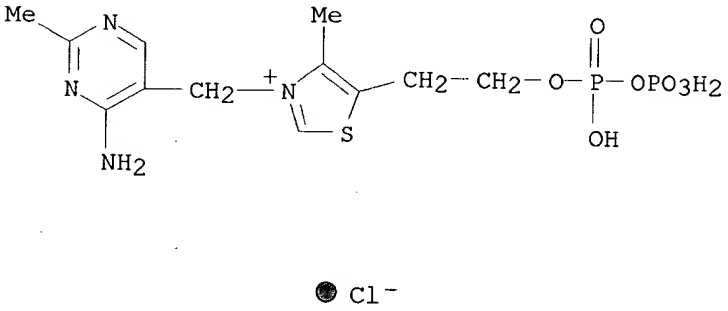
LANGUAGE: Russian

AB Thiamin, thiamin pyrophosphate, and 4-methyl-5-β-hydroxyethylthiazole are studied for their effect on the acetylcolinesterase activity in the brain, blood plasma, and erythrocytes. The activity of acetylcholinesterase in blood cells is inhibited most of all by thiamin and the thiazole. **Acetylcholinesterase** of the brain was inhibited only by thiamin **pyrophosphate**.

IT **154-87-0**, Thiamine **pyrophosphate**
RL: BIOL (Biological study)
(**acetylcholinesterase** of blood and brain response to)

RN 154-87-0 CAPLUS

CN Thiazolium, 3-[(4-amino-2-methyl-5-pyrimidinyl)methyl]-4-methyl-5-(4,6,6-trihydroxy-4,6-dioxido-3,5-dioxa-4,6-diphosphahex-1-yl)-, chloride (9CI) (CA INDEX NAME)



L15 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2003 ACS

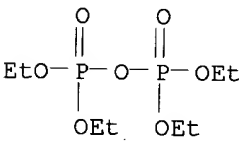
ACCESSION NUMBER: 1974:433248 CAPLUS

DOCUMENT NUMBER: 81:33248
TITLE: Anticholinesterase ability of diethyl S-propyl phosphorothiolate. Errors caused by the presence of an active impurity
AUTHOR(S): Gazzard, Michael F.; Sainsbury, Gordon L.; Swanston, Dennis W.; Sellers, David; Watts, Peter
CORPORATE SOURCE: Chem. Def. Estab., Salisbury, UK
SOURCE: Biochemical Pharmacology (1974), 23(3), 751-2
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Diethyl S-propyl phosphorothiolate (I) [20195-06-6] prepared by the method of P. Bracha and R. D. O'Brien (1968) contained an impurity, probably tetraethyl **pyrophosphate** [**107-49-3**], which increased markedly the apparent second order rate constant for inhibition of bovine erythrocyte **acetylcholinesterase** (EC 3.1.1.8) [9001-08-5] by I and decreased apparent LD50 in mice to a smaller extent. The results and conclusions of studies on the toxicities and anticholinesterase activities of diethyl alkyl phosphorothiolates by the above authors may be in error.

IT **107-49-3**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(anticholinesterase activity and toxicity of, as diethyl propyl phosphorothiolate impurity)

RN 107-49-3 CAPLUS
CN Diphosphoric acid, tetraethyl ester (9CI) (CA INDEX NAME)



L15 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1961:3812 CAPLUS
DOCUMENT NUMBER: 55:3812
ORIGINAL REFERENCE NO.: 55:780i,781a-c
TITLE: Cholinesterase inhibition and spontaneous activity of the frog rectus abdominis muscle
AUTHOR(S): Kraatz, C. P.
CORPORATE SOURCE: Jefferson Med. Coll., Philadelphia, PA
SOURCE: J. Pharmacol. Exptl. Therap. (1960), 130, 194-203
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

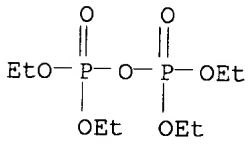
AB Inhibition of the cholinesterase of the isolated frog rectus abdominis muscle leads to spontaneous shortening. The effectiveness of various inhibitors in evoking such activity generally parallels their ability to sensitize the muscle to **acetylcholine**, with tetraethyl **pyrophosphate** (TEPP) most consistently active and neostigmine somewhat inferior. The property is manifested in varying degrees by unsym. diethyl bis(dimethylamido)pyrophosphate (B-6515), pyridostigmine, and edrophonium, while octamethyl pyrophosphoroamide and physostigmine are ineffective. Spontaneous contractions in 10-6 dilution TEPP or 10-5 B-6515 occur only after approx. 90% of the cholinesterase of the muscle has been inactivated. Localization expts. and inhibition by curare and other drugs that depress the responses to acetylcholine indicate that a fully sensitive neuromuscular junction is essential for development of the

activity. The twitch and tonus components are both brought into activity by minimal concns. of TEPP, while the other inhibitors at comparable levels activate principally twitch fibers.

IT **107-49-3**, Ethyl pyrophosphate, Et4P2O7
(cholinesterase inhibition by, muscle spontaneous activity and)

RN 107-49-3 CAPLUS

CN Diphosphoric acid, tetraethyl ester (9CI) (CA INDEX NAME)



L15 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1964:407045 CAPLUS

DOCUMENT NUMBER: 61:7045

ORIGINAL REFERENCE NO.: 61:1142h

TITLE: Effect of purines on the acetylcholine content of rat brain

AUTHOR(S): Bose, B. C.; Saifi, A. Q.; Ray, N. M.

CORPORATE SOURCE: M.G.M. Med. Coll., Indore

SOURCE: Current Sci. (India) (1964), 33(7), 212

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

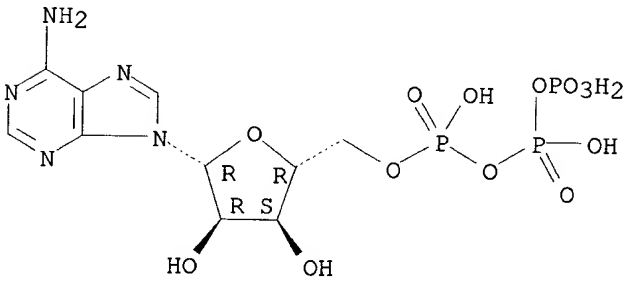
AB The average acetylcholine (I) content in brain tissue of control rats was 2.46 γ/g. The I content of the brain after acute administration of the following purine derivs. was: theophylline, 4.12 ± 0.12; theobromine, 2.48 ± 0.43; adenosine diphosphate, 2.06 ± 0.18; adenosine triphosphate, 1.83 ± 0.29; and caffeine, 1.60 ± 0.20 γ/g. On chronic administration, none of the above drugs influence the I level of brain tissue.

IT **56-65-5**, Adenosine triphosphate **58-64-0**, Adenosine **pyrophosphate**
(**acetylcholine** in brain after administration of)

RN 56-65-5 CAPLUS

CN Adenosine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

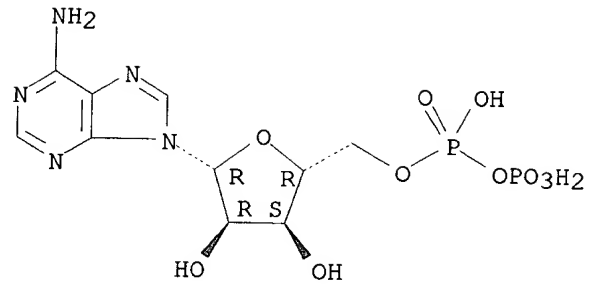
Absolute stereochemistry.



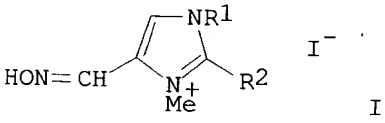
RN 58-64-0 CAPLUS

CN Adenosine 5'-(trihydrogen diphosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L15 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1985:20204 CAPLUS
DOCUMENT NUMBER: 102:20204
TITLE: Reactivators of organophosphorus-inhibited acetylcholinesterase. 1. Imidazole oxime derivatives
AUTHOR(S): Mar Herrador, M.; Saenz de Buruaga, Jesus; Dolores Suarez, M.
CORPORATE SOURCE: Fac. Farm., Univ. Granada, Granada, Spain
SOURCE: Journal of Medicinal Chemistry (1985), 28(1), 146-9
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

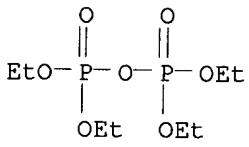


I

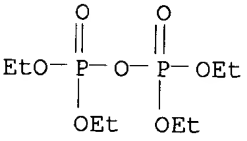
AB The title compds. I (R1 = Et, allyl, Ph, 4-EtOPh, 4-MeOPh, and 4-MePh; R2 = H or MeS) prepared by methylation of the appropriate 4-formylimidazole with MeI and subsequent condensation with NH2OH were tested for their reactivating potency on Electrophorus **acetylcholinesterase** inhibited by tetraethyl **pyrophosphate**. The results showed that I were weak reactivators of the enzyme. The 2 most active compds., 1-allyl-4-[(hydroxyimino)methyl]-3-methylimidazolium iodide (I; R1 = allyl, R2 = H) and (Z)-1-allyl-4-[(hydroxyimino)methyl]-3-methyl-2-(2-methylthio)imidazolium iodide (I; R1 = allyl, R2 = MeS), were .apprx.2-fold less active than 2-pyridine aldoxime methiodide (2-PAM). The MeS group at position 2 of the imidazole ring generally exerted a weak neg. effect on the reactivating properties. The reduction in reactivating activity in comparison with that of 2-PAM appeared to be due more to the low acidity of the hydroxyimino group than to a lack of structural requirements.

IT **107-49-3**
RL: BIOL (Biological study)
(acetylcholinesterase inhibited by, imidazole oxime derivative reactivation of)

RN 107-49-3 CAPLUS
CN Diphosphoric acid, tetraethyl ester (9CI) (CA INDEX NAME)



L15 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1959:57851 CAPLUS
DOCUMENT NUMBER: 53:57851
ORIGINAL REFERENCE NO.: 53:10508h-i
TITLE: Action of anticholinesterases on the bronchial muscle of the guinea pig: sensitization to acetylcholine and histamine
AUTHOR(S): Chary, R.; Bocquet, P.; Jayot, R.
CORPORATE SOURCE: Centre etudes Bouchet, Paris
SOURCE: J. physiol. (Paris) (1958), 50, 215-19
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C.A. 52, 18853g. In mg./kg. body weight concns. isopropyl phosphorofluoridate (0.010), eserine salicylate (0.025), ethyl phosphoramidocyanidate, and tetraethyl **pyrophosphate** (I) (0.025) augmented the bronchoconstrictor effect of **acetylcholine**. All except I sensitized the similar effect of histamine.
IT **107-49-3**, Ethyl **pyrophosphate**, Et4P2O7
(effect on bronchial constrictor effect of **acetylcholine** and histamine)
RN 107-49-3 CAPLUS
CN Diphosphoric acid, tetraethyl ester (9CI) (CA INDEX NAME)

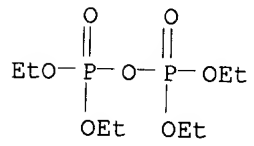


L15 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1960:69801 CAPLUS
DOCUMENT NUMBER: 54:69801
ORIGINAL REFERENCE NO.: 54:13406c-d
TITLE: Microchemical demonstration of the role of esterase-A during the hydrolysis in vivo of tetraethylpyrophosphate (TEPP)
AUTHOR(S): Crevier, Marc
CORPORATE SOURCE: Dept. Natl. Health & Welfare, Ottawa, Can.
SOURCE: Arch. intern. physiol. et biochim. (1958), 66, 489-55
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. CA 50, 16925e. Acetylcholinesterase (AChE) activity of the nerve motor end plates was determined by C.'s histophotometric method. In rats a prophylactic dose of aldrin (I) indirectly protected the peripheral cholinergic receptors, during acute and subacute TEPP poisoning, by accelerating the hydrolysis in vivo of TEPP by esterase-A. I alone had no effect on the AChE activity of the receptors.
IT **107-49-3**, Ethyl pyrophosphate, Et4P2O7

(hydrolysis of, by esterase A, alduin effect on, in acetyl-cholinesterase protection)

RN 107-49-3 CAPLUS

CN Diphosphoric acid, tetraethyl ester (9CI) (CA INDEX NAME)



L15 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1993:118823 CAPLUS

DOCUMENT NUMBER: 118:118823

TITLE: Rapid detection of anticholinesterase insecticides by a reusable light addressable potentiometric biosensor

AUTHOR(S): Fernando, John C.; Rogers, Kim R.; Anis, Nabil A.; Valdes, James J.; Thompson, Roy G.; Eldefrawi, Amira T.; Eldefrawi, Mohyee E.

CORPORATE SOURCE: Sch. Med., Univ. Maryland, Baltimore, MD, 21201, USA

SOURCE: Journal of Agricultural and Food Chemistry (1993), 41(3), 511-16
CODEN: JAFCAU; ISSN: 0021-8561

DOCUMENT TYPE: Journal

LANGUAGE: English

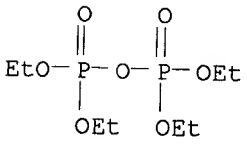
AB A light addressable potentiometric sensor (LAPS) was used to detect organophosphate and carbamate anticholinesterases (anti-ChEs), using eel acetylcholinesterase (AChE) as the biol. sensing element. Biotinylated AChE was preincubated with inhibitor or buffer alone and then captured on biotinylated nitrocellulose membrane via streptavidin crosslinking, or AChE was preimmobilized on the capture membrane and then sample containing the anti-ChE was filtered through the capture membrane. Hydrolysis of acetylcholine (ACh) by the captured AChE resulted in a strong potentiometric signal, and the immobilized AChE retained its affinity for ACh and anti-ChEs. IC50 values for inhibition of captured AChE obtained by the LAPS agreed with those obtained by a spectrophotometric method or a fiber optic evanescent fluorosensor. Paraoxon and bendiocarb were detected at 10 nM, while higher concns. were required for monocrotophos, dicrotophos, dichlorvos, phosdrin, diazinon, tetra-Et pyrophosphate, aldicarb, and methomyl. Important features of the LAPS for detection of anti-ChEs are speed (8 samples assayed simultaneously in minutes), precision, and reusability.

IT **107-49-3**, Tetraethyl **pyrophosphate**

RL: ANT (Analyte); ANST (Analytical study)
(determination of, by **acetylcholinesterase**-containing reusable light addressable potentiometric biosensor)

RN 107-49-3 CAPLUS

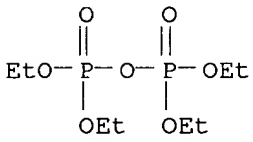
CN Diphosphoric acid, tetraethyl ester (9CI) (CA INDEX NAME)



L15 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1961:14838 CAPLUS
DOCUMENT NUMBER: 55:14838
ORIGINAL REFERENCE NO.: 55:2943d-e,2944a-b
TITLE: The role of esterase inhibition in tetraethylpyrophosphate poisoning in the housefly, Musca domestica
AUTHOR(S): Stegwee, D.
CORPORATE SOURCE: Pesticide Research Inst., London
SOURCE: Can. J. Biochem. and Physiol. (1960), 38, 1417-30
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB The effect of Et4P2O7 was studied on the in vivo activity of different esterases in the housefly. Et4P2O7 was found to cause inhibition of the acetylcholinesterase and of the aliesterase which hydrolyzes Et butyrate. The latter esterase could be selectively inhibited in vivo by treating the flies with tri-o-tolyl phosphate (TOCP). Typical symptoms of organophosphorus poisoning developed only after Et4P2O7 when acetylcholinesterase was inhibited. Inhibition of this enzyme coincided with a rise of the level of acetylcholine in the insects. Treatment with TOCP caused a lowering of the level of acetylcholine. The insects became less sensitive to subsequent treatment with Et4P2O7 and in this case showed a lesser degree of accumulation of acetylcholine. The importance of acetylcholinesterase and aliesterase in Et4P2O7 poisoning is discussed. It is concluded that the major biochem. lesion effected was the inhibition of acetylcholinesterase. Inhibition of the aliesterase was not directly related to the toxic action of Et4P2O7, although possibly it led to interference with the accumulation of acetylcholine resulting from the acetylcholinesterase inhibition.

IT **107-49-3**, Ethyl pyrophosphate, Et4P2O7
(esterase in fly response to)
RN 107-49-3 CAPLUS
CN Diphosphoric acid, tetraethyl ester (9CI) (CA INDEX NAME)



L15 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1960:56836 CAPLUS
DOCUMENT NUMBER: 54:56836
ORIGINAL REFERENCE NO.: 54:11114f-i,11115a
TITLE: The antagonism of some actions of tetraethylpyrophosphate by morin
AUTHOR(S): Balotin, N. Malcolm; Coon, J. M.
CORPORATE SOURCE: Jefferson Med. Coll., Philadelphia, PA
SOURCE: Arch. intern. pharmacodynamie (1960), 123, 395-405
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In cell-free exts., a number of flavonoid compds. were found inhibitory to choline acetylase, the enzyme involved in the final step of acetylcholine (I) synthesis, one of the most active in this respect being morin (II), 2',3,4',5,7-pentahydroxyflavone; since the latter exhibited a relatively

low toxicity, it was considered possible to achieve a sufficient concentration in vivo to reduce the production of I and thus modify the toxic action of cholinesterase (III) inhibitors. Tetraethylpyrophosphate (TEPP) was selected as the anticholinesterase agent against which the antagonistic actions of II have been tested. Pretreatment of Swiss Webster male mice, weighing 20-25 g., by II (injected intraperitoneally as an oil-in-H2O emulsion prepared by homogenizing II with 25 ml. of sesame oil and 25 ml. H2O plus 1 ml. of the emulsifying agent, sorbitan sesquioleate) 50-1000 mg./kg. body weight plus atropine (IV) significantly increased the L.D.50 of TEPP; neither II or IV alone exerted a significant effect. II and IV exerted additive toxic effects on mice. When the dose of IV was held constant at 100 mg./kg. body weight, the lethal effect of the combination appeared essentially as a II intoxication, while a II-IV combination of 2:1 manifested IV-like intoxication. II (injected intravenously in alkaline solution in rats at pH 8.7-8.9 in a volume of 0.10-0.15 ml./injection) suppressed muscular fasciculations produced in mice and rats by TEPP, sustained respiration and increased survival-time in atropinized, anesthetized rats poisoned with TEPP, antagonized the actions of TEPP and physostigmine on the isolated frog heart and of TEPP on the isolated rabbit ileum, but did not antagonize the action of I on these organs (in isolated tissues, II was dissolved with the aid of NaOH solution in the perfusing or bathing medium); II appeared to prevent or reverse certain effects of TEPP by enabling a reduction in I synthesis rather than by a IV-like mechanism, or by reactivation of III.

IT **107-49-3**, Ethyl pyrophosphate, Et4P2O7
(cholinesterase inhibition by, morin effect on)

RN 107-49-3 CAPLUS

CN Diphosphoric acid, tetraethyl ester (9CI) (CA INDEX NAME)